REMARKS

Claims 18 and 20-27 are pending. Claim 26 is withdrawn from further consideration. Claims 18, 20-25 and 27 are rejected. Reconsideration in light of the following remarks is requested.

Applicant has not dedicated nor abandoned any unclaimed subject matter. Moreover, Applicant has not acquiesced to any rejections or objections made by the Patent Office. Applicant reserves the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

Claim Rejections under 35 USC 103

Claims 18, 20, 24 and 27 are rejected under 35 USC 103(a) as allegedly being unpatentable over US Patent 6,319,670 to Sigal et al. ("*Sigal*") in view of US Patent 5,770,369 to Meade et al. ("*Meade*") and US Patent 5,958,791 to Roberts et al. ("*Roberts*").

Claim 21 is rejected under 35 USC 103(a) as allegedly being unpatentable over *Sigal* in view of *Meade*, *Roberts* and US Patent 5,620,850 to Bamdad et al. ("*Bamdad*").

Claim 22 is rejected under 35 USC 103(a) as allegedly being unpatentable over *Sigal* in view of *Meade*, *Roberts* and US Patent 5,565,658 to Gerpheide et al. ("*Gerpheide*").

Claims 23 and 25 are rejected under 35 USC 103(a) as allegedly being unpatentable over *Sigal* in view of *Meade*, *Roberts* and US Patent 6,096,273 to Kayyem et al. ("*Kayyem*").

1) The Graham Factors

When rejecting claims under 35 U.S.C. §103, the Examiner bears the initial burden of factually supporting any *prima facie* conclusion of obviousness. MPEP § 2142. The inquiry of obviousness is controlled by the Graham factors. See *KERR International Co. v. Teleflex Inc.* 1727 A.C.T. (2007) (citing *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1 (1966)). These factors are: 1) the scope and content of the prior art; 2) the differences between the prior art and the claims; 3) the level of ordinary skill in the pertinent art; and 4) objective evidence of nonobviousness.

A. Sigal

Sigal is directed to compositions and methods used to measure the presence of analyte by measuring electrochemiluminescence triggered by a voltage imposed on a working electrode. See col. 1, lines 15 – 19 and lines 48-49. In electrochemiluminescence assays, a reactive species is reduced and thus placed in an excited state. Upon relaxation, a photon is emitted and detected by a photomultiplier tube (PMT).

On page 3 of the Office Action mailed September 27, 2007 the Examiner concedes that "Sigal et al. do not disclose a substrate comprising an array of electrodes and a detector capable of detecting the voltage associated with electron transfer moiety… ."

B. Meade

Meade is directed to electron transfer via nucleic acids. The Examiner relies on *Meade* to provide the motivation for replacing the photon detector of *Sigal* with the "detector capable of detecting a voltage associated with electron transfer from said electron transfer moiety" as recited in the claims.

C. Roberts

Roberts is directed to a test device for detecting or determining an analyte in a test solution. The Examiner cites *Roberts* for its disclosure of the "advantage of fabricating small electrode in interdigitated arrays." Page 4 of Office Action mailed September 27, 2007.

First of all, the interdigitated arrays in *Roberts*, column 7, line 66 to column 8, line 26, as cited by the Examiner, are not arrays of working electrodes. *Roberts* states that "[a]dvantages of fabricating small electrodes in interdigitated array go even further by allowing redox cycling of ions back and forth between anode(s) and cathode(s)." This passage implies that the interdigitated array of *Roberts* comprises not working electrodes, but rather, one working electrode having multiple fingers interdigitated with one reference electrode also having multiple fingers.

D. Arguments

The Examiner concedes *Sigal* does not teach "an array of working electrodes." See page 9 of Office Action of September 27, 2007. However, the Examiner states that "the rejection … is based on the combination of patents … and is not on whether Roberts et al. teach working

electrode or not as argued by applicant." See page 10 of Office Action of September 27, 2007. Applicants respectfully disagree.

M.P.E.P. § 21.41III states:

> The prior art reference (or references when combined) need not teach or suggest all the claim limitations, however, Office personnel must explain why the difference(s) between the prior art and the claimed invention would have been obvious to one of ordinary skill in the art... . The gap between the prior art and the claimed invention may not be "so great as to render the [claim] nonobvious to one reasonably skilled in the art." (Citation omitted.)

Applicants contend that even assuming *arguendo* the combination of *Sigal*, *Meade* and *Roberts* do not teach or suggest the limitation of "an array of working electrodes," the gap between the prior art and the claimed invention is still so great as to render the pending claims nonobviousness to one reasonably skilled in the art.

First of all, as argued above, the interdigitated "arrays" in *Roberts* are not "arrays of working electrodes" as claimed.

Secondly, the advantages of "increasing the size of mass transport, increasing the signal-to-noise (faradaic/charging current) ratio, and decreasing ohmic signal losses" are in reference to the small scale of the *Roberts* electrodes, rather than to any configuration of working arrays.

Thirdly, as presented in more detail below, the principle of operation of *Sigal* is different from that of the claimed invention. *Sigal* depends on the detection of photons; the pending claims are directed to detection of a voltage. The combination of *Sigal*, *Meade*, and *Roberts* would change the principle of operation of *Sigal*, render compositions and methods for conducting electrochemiluminescence binding assays of *Sigal* unsatisfactory for their intended purpose.

Finally, as outlined below, there is no a reasonable expectation of success by combining *Sigal* in view of *Meade*.

Thus the gap between the combination of *Sigal, Meade*, and *Roberts* and the claimed invention is still so great as to render the pending claims nonobviousness to one reasonably skilled in the art. Accordingly, the Examiner has failed to establish a *prima facie* case of obviousness. Applicants request withdrawal of the rejection under 103(a) of claim 18 and claims 20-25 and 27 dependent therefrom.

D. Bamdad

Claim 21 is rejected under 35 USC 103(a) as allegedly being unpatentable over *Sigal* in view of *Meade*, *Roberts* and *Bamdad*. The Examiner claims that *Bamdad* teaches a self-assembling monolayer that is made by alkyl thiol functional groups.

As argued herein, claim 18 is not obvious over *Sigal* in view of *Meade* and *Roberts*. *Bamdad*, directed toward derivatized surfaces for surface plasmon resonance experiments, does not cure the deficiencies of the references. Therefore, not all of the limitations of claim 21 are found in the cited references, and so a prima facie case of obviousness has not been established for claim 21. Applicants request withdrawal of the rejection.

E. Gerpheide

Claim 22 is rejected under 35 USC 103(a) as allegedly being unpatentable over Sigal in view of *Meade*, *Roberts* and *Gerpheide*.

As argued herein, claim 18 is not obvious over *Sigal* in view of *Meade* and *Roberts*. *Gerpheide*, directed to apparatus and method for a capacitance-based proximity sensor with interference rejection, does not cure the deficiencies of the references. Therefore, not all of the limitations of claim 21 are found in the cited references, and so a *prima facie* case of obviousness has not been established for claim 21. Applicants request withdrawal of the rejection.

F. Kayyem

Under 35 U.S.C. § 103(c)(1), *Kayyem* cannot preclude patentability of the presently claimed invention under U.S.C. § 103.

35 U.S.C. § 103(c)(1) states:

> [s]ubject matter developed by another person, which qualifies as prior art only under one or more of subsections (e), (f), and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the claimed invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Kayyem cannot be used in an obvious rejection under 35 U.S.C. § 103(a) if the reference could only qualify as prior art under 35 U.S.C. § 102(e), (f), or (g), and was owned by the same entity or subject to an obligation of assignment to the same entity as the instant application at the time the claimed invention was made.

1. Because *Kayyem* is not a prior art reference under 35 U.S.C. §§ 102(a), (b), (c), or (d), *Kayyem* could only be alleged prior art under 35 U.S.C. §§ 102(e), (f), or (g).

Kayyem is not prior art under 35 U.S.C. § 102(a) because it was published on August 1, 2002, well after the filing date and priority date of the instant application. Likewise, *Kayyem* is not a prior art reference under 35 U.S.C. § 102(b) because *Kayyem* was not published or issued more than one year before the priority date of the instant application. *Kayyem* is also not a prior art reference under 35 U.S.C. § 102(c) or (d). Therefore, *Kayyem* could only be considered as alleged prior art under 35 U.S.C. §§ 102(e), (f), or (g).

2. Statement of Common Ownership.

In accordance with the requirements to establish common ownership articulated in M.P.E.P. § 706.02(l)(2), the instant U.S. Patent Application No. 10/016,416 and the *Kayyem* patent were, at the time the invention of the instant application was made, owned by Clinical Micro Sensors, Inc.

Therefore, according to U.S.C. § 103(c)(1), *Kayyem* cannot preclude patentability of the presently claimed invention under U.S.C. § 103. Because this ground for rejection is improper, Applicants respectfully request that it to be withdrawn.

2) There is no motivation to combine *Sigal* with *Meade*, *Roberts*, or *Gerpheide* to reach the claimed invention

"[A] patent composed of several elements is not proved obviousness merely by demonstrating that each of its elements was, independently, known in the prior art.... [I]t can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *KSR*, at 1743.

A. The proposed modification or combination of *Sigal* with other references would change the principle of operation of *Sigal.*

If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims prima facie obvious. *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959), M.P.E.P. § 2143.02 VI.

The Examiner concedes that "Sigal et al. do not disclose ... a detector capable of detecting the voltage associated with electron transfer moiety as recited in a) and c) of claim 18." Page 3 of the Office Action mailed September 27, 2007. The Examiner relies on *Meade* to provide the motivation for replacing the photon detector of *Sigal* with the "detector capable of detecting a voltage associated with electron transfer from said electron transfer moiety" as recited in the claims. The Examiner states in page 9 of the Office Action mailed September 27, 2007 that:

> [A]lthough the examiner agrees with applicants that "[A] voltage detector does not detect photon"... the detector capable of detecting the integrated photocurrent associated with electron transfer moiety taught by *Sigal et al.*, and the detector capable of detecting the voltage associated with electron transfer taught by Meade et al., are used for the same purpose (ie. detecting electron transfer of the transitional metal complex), the detector taught by Sigal *et al.*, and the detector taught by Mead et al., are exchangeable in order to detect electron transfer of the transitional metal complex.

Thus, the Examiner assumes that the principle of operation of *Sigal* is "to detect electron transfer of the transitional metal complex." Applicants respectfully disagree.

Principle is defined as "the laws or facts of nature underlying the working of an artificial device." Merriam –Webster Online Dictionary (www.m-w.com). Thus the principle of operation for the invention disclosed in *Sigal* should be "the laws or facts of nature underlying the working of [the] artificial device" disclosed in *Sigal*.

The title of *Sigal* is "Methods and Apparatus for Improved Luminescence Assays Using Micropaticles." In the section tiled "Filed of the Invention" *Sigal* states:

> This application relates generally to methods and compositions for conducting binding assays, more particularly to those which measure the presence of an analyte of interest by measuring ***electrochemiluminescence*** emitted by one or more labeled components of the assay system. (Emphasis added.)

Col. 1, ll. 15-19.

In the section titled "Objects of the Invention" *Sigal* further states: "a ***primary object*** of this invention to provide methods, reagents and compositions, for conducting of ***electrochemiluminescence*** binding assays." (Emphasis added.) Col. 2, ll. 12-23.

In the *section* titled "Summary of the Invention" *Sigal* states that:

> These and other objects of the invention are achieved using microparticles comprised of an electrically conductive material having (a) one or more copies of an assay ligand immobilized on its outer surface, and (b) a plurality of ***electrochemiluminescent moieties*** immobilized on its outer surface. The assay ligand may be linked to the ***electrochemiluminescent moiety***. More specifically, it has now been found that colloidal gold is a highly advantageous conductive material with which to form microparticles. Colloidal gold particles having one or more assay ligands immobilized on its outer surface and a plurality of ***ECL moieties*** immobilized on its outer surface can be used in a wide range of assay formats, including those based on ***detecting the ECL*** from moieties immobilized on the particle and those based on the modulation by the particles of the ***ECL from free ECL moieties in*** solution. The objects of the present invention may also be achieved using microparticles that do not comprise electrically conductive material. (Emphasis added.)

Col. 2, ll. 46-64.

Thus, the plain language of *Sigal* itself shows that the "artificial device" disclosed in *Sigal* are "reagents and compositions, for conducting of electrochemiluminescence binding assays." As such, the principle of operation of the *Sigal* inventions is the laws or facts of nature underlying the working of reagents and compositions for conducting of electrochemiluminescence binding assays. Therefore, the principle of operation is the detection of "electrochemiluminescence," NOT the detection of "electron transfer of the transitional metal complex."

This is further evidenced by the issued claims of *Sigal*. All the claims recite in the preamble either "[a] method for conducting e***lectrochemiluminescence*** measurements," or "[a] method for performing an ***electrochemiluminescence*** binding assay." All the issued claims also require the step of "conducting an ***electrochemiluminescence*** measurement [] in the presence of ***electrochemiluminescence*** reactants." (Emphasis added.) Nowhere in *Sigal* can the term "electron transfer" be found.

Accordingly, even assuming for the sake of argument that the Examiner has met his burden of presenting a *prima facie* case of obviousness, Applicants have rebutted any *prima facie* case of obviousness by showing that modification of the primary reference would change the principle of its operation.

Because claim 18 is not obvious over the combination of the cited references, Applicants request withdrawal of the rejection under 103(a) of claim 18 and claims 20-25 and 27 dependent therefrom.

B. The proposed modification of *Sigal* in view of *Meade* would render compositions and methods for conducting electrochemiluminescence binding assays of *Sigal* unsatisfactory for their intended purpose.

Because the detector of claim 18 does not detect photons, ligand binding according to *Sigal* could not be detected. Accordingly, the compositions and methods for conducting electrochemiluminescence binding assays of *Sigal* would not achieve their intended purpose if the detector of claim 18 replaced the photomultiplier tube in *Sigal*.

Accordingly, even assuming for the sake of argument that the Examiner has met his burden of presenting a *prima facie* case of obviousness, Applicants have rebutted any *prima facie* case of obviousness by showing that modification of the primary reference would it unsatisfactory for its intended purpose.

C. There is no a reasonable expectation of success by combining *Sigal* in view of *Meade*.

The Supreme Court also held in *KSR* that, "The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." *KSR*, at 1739. Thus evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness. *In re Rinehart*, 531 F.2d 1048 (CCPA 1976). The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680 (Fed. Cir. 1990). MPEP. § 2143.01.

As presented above, the detector of claim 18 does not detect photons, ligand binding according to *Sigal* could not be detected. Accordingly, there is no a reasonable expectation of success by combining *Sigal* in view of *Meade*.

D. *Gerpheide* explicitly teaches away from *Roberts*

"[W]hen the prior art teaches away from combining certain known elements, discovery of a successful means of combining them is more likely to be nonobvious." *KSR*, at 1740. "[A]

reference may teach away when a person skilled in the art, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant." *In re ICON*, at 1751.

Assuming *arguendo* that *Roberts* teaches an array of working electrodes, *Roberts* teaches at column 5, lines 32-34, that its device "includes an absorbent material, having a contact portion proximate to one end for contact with and uptake of the test solution." Each of the conductors in *Roberts* "comprises a plurality of fingers disposed on the absorbent material." *Id.* at lines 37-38. Absorbent material means

> a porous material having a pore size of from 0.05 μm to 50 μm, preferably from 0.45 μm to 5 μm, which is susceptible to traversal by an aqueous medium in response to capillary force. Such materials may be natural polymeric materials, particularly cellulosic materials, such as fiber-containing papers, . . . [and] synthetic or modified naturally occurring polymers, such as nitrocellulose. . . . Nitrocellulose is a preferred absorbent material.

Id. at col. 12, lines 3- 15.

Gerpheide, however, teaches at column 5, lines 28-30, that "the electrode array may utilize a flexible printed circuit board, such as a flex circuit, or stampings of sheet metal or metal foil." One of skill in the art would understand that sheet metal and metal foil are not absorbent materials. Furthermore, one of skill in the art would understand that substrates used in flex circuits are preferably not absorptive. See Joseph Fjelstad, Flexible Circuit Technology 43 (3d ed. 2007) (attached as Exhibit A in the previous response; "Moisture absorption is definitely not desirable for any flexible substrate. Moisture can negatively impact both the manufacturing process (by causing delamination, in process or in assembly) and the performance of the finished product (by altering the material's dielectric constant and increasing signal loss.)")

Therefore, *Gerpheide* explicitly teaches away from *Robers* because *Roberts* teaches that its device "includes an absorbent material," and in contrast, *Gerpheide* teaches that the electrode array may utilize a flexible printed circuit board, such as a flex circuit, or stampings of sheet metal.

CONCLUSION

Applicants believe the claims are in a condition for allowance. Early notification thereof is respectfully requested. The Examiner is invited to call the undersigned at 415.442.1000 to resolve any questions. Although Applicants do not believe any fees are required, the Commissioner is authorized to charge any additional fees that may be required, including extension fees or additional claim fees, or to credit any overpayment to Deposit Account No. 50-0310 (Docket No. 067456-5020-US01).

Respectfully submitted,

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Dated: February 27, 2008

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